UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,048	05/12/2006	Keiji Kubo	08279.1211USWO	3633

52835 7590 12/10/2007

HAMRE, SCHUMANN, MUELLER & LARSON, P.C.
P.O. BOX 2902
MINNEAPOLIS, MN 55402-0902

EXAMINER	
LOEWE, SUN JAE Y	

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,048	KUBO ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *2,14 and 20-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 19* is/are rejected.

7)☒ Claim(s) *1,3-13 and 15-17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

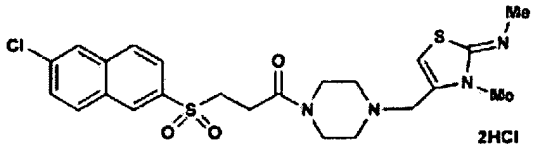
1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9-12-2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-25 are pending in the instant application.

Election/Restrictions

2. Applicant's election without traverse of Group I (claims 1, 3-13 and 15-19) and species of Example 5 (see structure below) in the reply filed on October 29, 2007 is acknowledged.



3. Claims 2, 14 and 20-25 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Election was made **without** traverse in the reply filed on October 29, 2007.

4. The search and examination of claims 1, 3-13 and 15-19 was performed for the elected species. MPEP 1893.03(d) states that when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. The elected invention (ie. species of Example 5) was not allowable under 35 U.S.C 112 (see below section 8). Thus, the nonelected subject matter (ie. non-elected species encompassed by Markush Formula I) was *not* rejoined for the present examination.

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on September 12, 2006 was filed in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. The IDS was considered. A signed copy of form 1449 is enclosed herewith.

Claim Objections

7. Claims 1, 3-13 and 15-19 objected to for containing non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 18 and 19 rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for the following intended use:

a) Anticoagulant (instant specification p. 276, Example 3);
b) Activated blood coagulation factor X inhibitor, ie. Factor Xa inhibitor (instant specification p. 273-276, Examples 1 and 2);
c) Treatment (not prophylactic) of deep vein thrombosis

The specification is not enabling for the scope of intended uses claimed (ie. intended uses beyond those noted above). Thus, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims
Claims are drawn to pharmaceutical composition comprising compound of Example 5 with a broad range of intended uses that include: treatment/prevention of myocardial infarction; prevention of deep vein thrombosis; treatment/prevention of thromboembolism during and post operation.

The nature of the invention
Intended use claimed is based on the inhibition of Factor Xa and the following in vitro/in vivo studies: anticoagulation, venous antithrombotic effect, and murine model of deep vein thrombosis.

The state of the prior art/level of ordinary skill/level of predictability

- The state of the art for the treatment/prophylaxis of the conditions/diseases claimed is unpredictable. See representative facts below:

  A. The two types of thrombosis (blood clots), venous (blood clot in the vein) and arterial (blood clot in the artery), are different in several aspects:

a. Symptoms, treatment, risk factor (Lifeblood, The Thrombosis Charity fact sheet for Venous Thrombosis and Arterial Thrombosis)

b. Etiology:
   - For example, shear conditions (Orvim et al. p. 12, Fressinaud et al. abstract)
   - Arterial thrombus formation at high shear conditions appears to be dependent on factor VIIa and thrombin-independent (Orvim et al. p. 12)
   - At venous shear conditions thrombus formation appears to be thrombin-dependent (Fressinaud et al., p. 993, 1st column)
   - *Note:* Factor Xa inhibition inhibits thrombin formation (Orvim et al., p. 2)

The instant specification provides support for venous thrombus formation. However, in view of the above, this disclosure does not support a correlation between the instant activity and arterial thrombus formation.

Myocardial infarction is a condition resulting from the blockage of arteries (http://www.answers.com/topic/myocardial-infarction?cat=health). Therefore, a correlation cannot be drawn between the instant activity and the treatment/ prevention of myocardial infarction.

B. The art recognized protocol for the prevention of deep vein thrombosis (eg. for "economy class syndrome") includes: medication, wearing of compression stockings, exercize, hydration and avoidance of alcohol/caffeine (http://www.webmd.com/heart-disease/tc/deep-vein-thrombosis-topic-overview?page=2).

Thus, it is art recognized that deep vein thrombosis arising from economy class syndrome is preventable. However, a correlation is only recognized for economy class syndrome DVT. Moreover, the correlation is between a combination of measures and not a single measure – eg. by medication.

Based on the above, a correlation cannot be drawn between the instant activity and the prevention of deep vein thrombosis.

C. The state of the art from the treatment/prevention of thromboembolism after operation is unpredictable (Lieberman et al., abstract; Paiement et al., abstract). Moreover, the protocol varies depending on the type of surgery (eg. total hip replacement vs. knee arthroplasty).

A correlation exists in the art between treatment (not prophylactic) of thromboembolism after total hip surgery and the use of anticoagulants. However, this correlation neither extends to the full scope of "surgery/operation", nor the to prophylaxis of any surgery/operation.

- An art recognized correlation is limited to the following: the instant activity and the treatment of deep vein thrombosis; or the instant activity and the treatment of thromboembolism due to hip replacement surgery. Thus, an art recognized correlation cannot be drawn between the instant activity and the scope of diseases claimed.

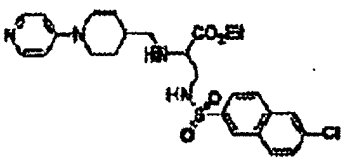
The amount of direction provided by the inventor/existence of working examples
The working examples support the intended use defined above, namely:

a) Anticoagulant (instant specification p. 276, Example 3);
b) Activated blood coagulation factor X inhibitor, ie. Factor Xa inhibitor (instant specification p. 273-276, Examples 1 and 2);
c) Treatment (not prophylactic) of deep vein thrombosis

The quantity of experimentation needed to make or use the invention
A correlation exists in the art between the instant activity and the intended uses above. However, this correlation does not extend to the scope of the intended use claimed. One of ordinary skill would thus not be enabled by the instant disclosure to practice the invention commensurate in scope with the claims.

Allowable Subject Matter

9. The following is a statement of reasons for the indication of allowable subject matter. The compound of Example 5 is novel and non-obvious over the art of record. The closest prior art is, for example, the disclosure of Eiko et al. (JP 2001011071) which teaches the compound



Conclusion

10. No claims allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sun Jae Y. Loewe
Art Unit 1626